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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,803	10/19/2001	Francis Blanche	03804.0135-02000	6741

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EXAMINER

PRIEBE, SCOTT DAVID

ART UNIT	PAPER NUMBER
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1632

DATE MAILED: 12/17/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.  
**09/981,803**

Applicant(s)  
**Blanche et al.**

Examiner  
**Scott D. Priebe, Ph.D.**

Art Unit  
**1632**



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-54 is/are pending in the application.
- 4a) Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3, 6-11, 14-17, 19-24, 26-30, 34-38, 42-46, 48, and 49 is/are rejected.
- 7) ☒ Claim(s) 4, 5, 12, 13, 18, 25, 31-33, 39-41, 47, and 50-54 is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on Feb 5, 2002 is/are a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some\* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☒ Certified copies of the priority documents have been received in Application No. 08/894,511.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 8 6) ☐ Other:

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## DETAILED ACTION

### *Priority*

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119 (a)-(d). The certified copy has been filed in parent Application No. 08/894,511, filed on 8/19/1997.

Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(a)-(d) based upon application FR 95 02117 filed in France by inventor Crouzet, Scherman, Cameron, and Wills. A claim for priority under 35 U.S.C. 119(a)-(d) cannot be based on said application, since the instant United States application was filed by inventor Cameron and Blanche, which is a different inventorship than the French application. See MPEP 201.13, especially the section labeled "(B)" immediately following the reproduction of 35 USC 119 and 37 CFR 1.55, and the section labeled "C. Identity of Inventors".

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

- a) An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

The status of 09/655,728 should be updated, and 08/894,511 should be identified as being --a 371 application of PCT/FR96/00274, filed 02/21/96, not published in English--.

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b) The second application must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the second application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

With respect to the subject matter of instant claims 4, 12, 18, 25, 31-33, 39-41, 47 and 50-54, none of the priority applications describe using the specific minicircles, plasmids or strains recited in the instant claims, nor the method of production of minicircles where both the minicircle region and the remaining section of the plasmid comprise a triple helix binding region. With respect to the subject matter of instant claims 9-11, 14-16, 23, 24, 26-28, 42-44, 48, and 49, none of the priority applications disclose using attL or attR sequences as the repeated sequences flanking the expression cassette, and excisionase in addition to integrase for resolution. With respect to the subject matter of instant claims 38 and 46, none of the priority applications disclose using the pBAD promoter for controlling expression of the integrase.

### ***Specification***

The disclosure is objected to because of the following informalities:

The title sheet (page 1) of the specification indicates that Crouzet, Scherman, Wils, and Darquet are inventors, and Blanche is not indicated as an inventor. This indication of inventorship does not agree with the declaration.

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Appropriate correction is required.

***Claim Objections***

Claim 43 is objected to because of the following informalities: in line 3, the “at” following “containing” should be deleted. Appropriate correction is required.

Applicant is advised that should claims 4 and 12 be found allowable, claims 5 and 13, respectively, will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k). Claims 4 and 12 limit the DNA to specific constructs, each of which has either SEQ ID NO: 12 or 13. Claims 5 and 13 simply recite a limitation which these DNAs already have. It is suggested that claims 4 and 12 should depend from claims 5 and 13.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 20, 24, 26, and 29 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 20, 26, the phrase "tRNA suppressor (supPhe)" renders the claim indefinite because it is unclear whether the claim is directed to any tRNA suppressor or only to a supPhe. See MPEP § 2173.05(d).

Claim 24 recites the limitation "said polynucleotide" in line 3. There is insufficient antecedent basis for this limitation in the claim.

Claim 29 recites the limitation "the recombinant DNA" in line 1. There is insufficient antecedent basis for this limitation in the claim.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-

(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published

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under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

(f) he did not himself invent the subject matter sought to be patented.

Claims 1-3, 6-8, 17, 19- 22, 29, 30, and 34-37 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Crouzet et al. 6,143,530 or Crouzet et al. US 6,492,164; and are rejected under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter.

The '164 patent is a division of the '530 patent, and except for the claims, the disclosures are identical. The subject matter of the instant claims is disclosed throughout both specifications and is claimed in the '530 patent, see for example claims 1-18, 24, 25, 28-37.

Claims 23 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Black (Gene 46: 97-101, 1986).

See Fig. 1, which discloses a plasmid comprising attR and attL flanking an expression cassette, wherein the expression cassette would be the Tc or Amp resistance in one part of the cointegrate or any of the  $\lambda$  genes of the other part of the cointegrate. The plasmid ori and marker genes are outside of the  $\lambda$  section of the cointegrate, and thus meeting the limitations of claim 24.

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Claims 23, 24 and 26 are rejected under 35 U.S.C. 102(b) as being anticipated by Peredelchuk et al. (Gene 187 (2): 231-238, 18 March 1997).

Peredelchuk discloses plasmids comprising an expression cassette positioned between  $\lambda$  attR and attL sequences, and a marker gene and ori outside the att sequences (relative to the expression cassette (see Fig. 3 C & D). pMP953 comprises *cat* expression cassette between the att sequences and a ColE1 *ori* and kanamycin resistance gene (*aph*) outside the att sequences. pMP954 has an *aph* expression cassette between the att sequences, with a ColE1 *ori* and *bla* (Amp<sup>R</sup>) selection marker outside the att sequences.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).



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Claims 9-11, 14-16, 23, 24, 26-28, 42-44, 48, and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouzet et al. 6,143,530 or Crouzet et al. US 6,492,164 as applied to claims 1-3, 6-8, 17, 19-22, 29, 30, and 34-37 above, and further in view of Backman, EP 0160571.

The Crouzet patents have been described above. They do not teach to use the attR and attL sequences in place of the attB and attP sequences, and include the excisionase.

However, Backman disclosed a system for making a variety of desired recombinant molecules in *E. coli* using the phage  $\lambda$  integration/excision system, including minicircles. Backman disclosed that either attB and attP could be used with the integrase or that attL and attR could be used with the integrase and excisionase. See page 4, line 12 to page 5, line 14; page 7- page 9, line 11; Figs. 4 and 5; claims 1, 2, 7-10.

Therefore, it would have been obvious to one of skill in the art at the time the invention was made to have replaced the attB and attP sequences with the attR and attL sequences and added the excisionase, since Backman taught that either was suitable for producing the desired recombinants.

Claims 34-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouzet et al. 6,143,530 or Crouzet et al. US 6,492,164 as applied to claims 1-3, 6-8, 17, 19- 22, 29, 30, and 34-37 above, and further in view of Bigger et al. (J. Biol. Chem. 276 (25): 23018-23027, 22 June 2001).

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Claims 42-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouzet et al. 6,143,530 or Crouzet et al. US 6,492,164 each further in view of Backman, EP 0160571 as applied to claims 9-11, 14-16, 23, 24, 26-28, 42-44, 48, and 49 above, and further in view of Bigger et al. (J. Biol. Chem. 276 (25): 23018-23027, 22 June 2001).

The Crouzet patents and Backman have been described above. The Crouzet patents taught to use a chemically-induced promoter for expression of the integrase (see '530 at col. 8, lines 3-17), but not the pBAD promoter.

However, Bigger disclosed that for efficient production of minicircles, currently available promoters were too leaky, and taught to use the pBAD system to more tightly control the expression of integrase.

Therefore, it would have been obvious to one of skill in the art at the time the invention was made to have used the pBAD promoter to control expression of the integrase and excisionase, because Bigger taught that previously used promoters were too leaky, and the pBAD promoter was more tightly controlled.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

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A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 6-8, 17, 19-22, 29, 30, 34-37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18, 24, 25, 28-37 of U.S. Patent No. 6,143,530. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are limited to some of the explicitly claimed embodiments of the '530. The instant claims simply omit other subject matter being claimed in the patent.

Claims 9-11, 14-16, 23, 24, 26-28, 42-44, 48, and 49 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18, 24, 25, 28-37 of U.S. Patent No. 6,143,530 in view of Backman, EP 0160571. The patent claims are directed to minicircles where the initial repeated sequences were attP and attB, but not attL and attR, which are both chimeric recombination products resulting from recombination between attP and attB.

However, Backman disclosed a system for making a variety of desired recombinant molecules in *E. coli* using the phage  $\lambda$  integration/excision system, including minicircles.

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Backman disclosed that either attB and attP could be used with the integrase or that attL and attR could be used with the integrase and excisionase. See page 4, line 12 to page 5, line 14; page 7- page 9, line 11; Figs. 4 and 5; claims 1, 2, 7-10.

Therefore, it would have been obvious to one of skill in the art at the time the invention was made to have replaced the attB and attP sequences with the attR and attL sequences and added the excisionase, since Backman taught that either was suitable for producing the desired recombinants.

Claims 34-38 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 37 of U.S. Patent No.6,143,530 in view of Bigger et al. (J. Biol. Chem. 276 (25): 23018-23027, 22 June 2001).

Claims 42-46 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 34 and 37 of U.S. Patent No.6,143,530 and Backman, EP 0160571 as applied to claims 42-45 above, and further in view of Bigger et al. (J. Biol. Chem. 276 (25): 23018-23027, 22 June 2001).

Claim 37 of the '530 patent requires the integrase to be under control of an inducible promoter, which in light of its specification includes chemically-inducible promoters. However, the pBAD promoter system is neither claimed nor disclosed. Backman also fails to teach the pBAD promoter.

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However, Bigger disclosed that for efficient production of minicircles, currently available promoters were too leaky, and taught to use the pBAD system to more tightly control the expression of integrase.

Therefore, it would have been obvious to one of skill in the art at the time the invention was made to have used the pBAD promoter to control expression of the integrase and excisionase, because Bigger taught that previously used promoters were too leaky, and the pBAD promoter was more tightly controlled.

Claims 1-3, 7 and 8 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 of U.S. Patent No. 6,492,164. Although the conflicting claims are not identical, they are not patentably distinct from each other because when the '164 claims are read in light of the specification, attB and attP sites are the preferred and exemplified site-specific recombination sequences, and these patent claims would clearly be considered to cover these sequences.

***Allowable Subject Matter***

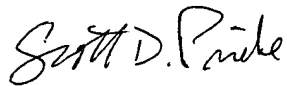
Claims 4, 12, 18, 25, 31-33, 39-41, 47 and 50-54 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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Certain papers related to this application may be submitted to Art Unit 1632 by facsimile transmission. The FAX numbers are (703) 308-4242 or (703) 305-3014 for any type of communication. In addition, FAX numbers for a computer server system using RightFAX are also available for communications before final rejection, (703) 872-9306, and for communications after final rejection, (703) 872-9307, which will generate a return receipt. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant *does* submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Scott D. Priebe whose telephone number is (703) 308-7310. The examiner can normally be reached on Monday through Friday from 8 AM to 4 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached on (703) 305-4051.

Any inquiry concerning administrative, procedural or formal matters relating to this application should be directed to Patent Analyst Patsy Zimmerman whose telephone number is (703) 308-8338. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.



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Art Unit 1632